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EDITORIAL

Endocrinology of Acne

The persistence of acne in a woman frequently evokes a concern for the presence of a hormonal abnormality to explain it, especially when the disease is unusually chronic and recalcitrant to treatment. The perception of a possible association is not difficult to understand, as acne activity often fluctuates in relation to the menstrual cycle and can be a sign of hyperandrogenism in ovarian and adrenal disorders. In the latter circumstances, though, there are almost always other manifestations of androgen excess, such as hirsutism and/or irregular menses, particularly oligomenorrhea.

A still unanswered question, however, has been whether acne, unaccompanied by hirsutism, menstrual irregularities, or other signs of virilism, can nonetheless be attended by endocrine dysfunction of a sufficient degree to aggravate and maintain the acne at a higher level of activity. Studies trying to demonstrate such a relationship have not been wanting, and, in fact, extend back more than four decades to the time when attempts were made to show (unsuccessfully) that urine extracts from acne patients were more active than normal when bioassayed for their androgenic effects in animals.

In more recent years, the advent of new and improved techniques for assaying hormones in biologic fluids has rekindled an interest in the possibility of detecting hormonal abnormalities in acne. From the results of such studies, an unequivocal picture of a consistent pattern of abnormal endocrine function has not emerged. To appreciate the uncertainty in this regard, one has only to peruse the various reports of the measurement of serum or plasma testosterone in women with acne in whom levels have been found to be normal (most often), slightly increased (less often), or increased (least often). There are similarly variable findings for the measurement of most other hormones.

What accounts for the discrepant findings among investigators? Some factors can be cited, such as too few patients studied, inadequate or inappropriate control groups, failure to indicate the presence or absence of other virilizing signs or symptoms, lack of information concerning time of blood sampling in relation to the menstrual cycle, and imprecision or insensitivity of analytical techniques. Inattention to one or more of these factors has undoubtedly been responsible, in part, for the disparity of the results obtained.

In this issue of the Journal, Lucky and her associates have reported on an extensive survey of the measurement of androgens and androgen precursors in the blood of women with acne. They have sorted out patients found to have both acne and hirsutism from those with acne alone and those with hirsutism alone. The nonacne control group of women were age-matched and examined to assure the absence of either of these physical characteristics. These investigators' findings show clearly enough that in women with acne alone, as compared to nonacne subjects, there are statistically significant increases in virtually all plasma androgens such as testosterone and dehydroepiandrosterone sulfate, and in androgen precursors such as 17α-hydroxyprogesterone. However, it should be stressed that these are differences of mean levels, and that with each hormone examined there is considerable overlap of individual values between the acne and normal groups. For example, only 12% of the acne patients actually had testosterone levels that exceeded the upper limit of normal. Even though an important observation was made—that the free or unbound level of testosterone, that small fraction of the circulating hormone which is the active form that enters the peripheral cell, was abnormally increased in 25% of the acne subjects—that still left 75% of patients who had normal levels.

In fact, for each of the hormones tested, there were always more acne patients with normal values than with abnormal values. The obvious thought, then, is that there may be two types of acne in women, i.e., endocrine acne and nonendocrine acne, despite the absence of signs other than acne to indicate a hyperandrogenic milieu. But there are no clinical clues that would allow us at the present time to distinguish one such group from the other, nor is there incontrovertible evidence that correction of abnormal hormone levels will reduce acne activity. Marynick and coworkers reported at the Endocrine Society meeting in 1981 that a high proportion of women and men with acne have increased serum dehydroepiandrosterone sulfate levels and that treatment with dexamethasone in very small doses, 0.25–0.375 mg daily, led to improvement of the acne in many cases. However, no placebo-treated group of patients was studied.

One might also speculate whether lowering of normal androgen levels by endocrine treatment to still lower levels might be just as beneficial as when there are abnormalities to begin with. Complicating any interpretation of the mechanism of such responses is the matter of peripheral metabolism by the skin of the hormones reaching it. One can imagine, for example, a circumstance in which an acne patient with active skin metabolism of androgens but with normal blood androgen levels might actually be in greater hormonal "imbalance" than an individual with heightened androgen blood levels but with relative androgen insensitivity of the skin. Future research endeavors should be directed not only to a further delineation of the scope of endogenous hormonal abnormalities in patients with acne but also to a knowledge of how these relate to peripheral cellular events. Only then is it likely that hormonal therapy can be targeted in a more rational manner so as to result in a reasonably predictable clinical response.

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